IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Michael J. Briskin		
Application No.:	08/875,849	Group:	1644
Filed:	September 8, 1997	Examiner:	R. Schwadron, Ph.D.
Confirmation No:	4411		
For:	MUCOSAL VASCULAR ADDRESSINS AND USES THEREOF		

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REPLY BRIEF

MS Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Reply Brief is being filed in response to the Examiner's Answer mailed from the U.S. Patent and Trademark Office on November 16, 2006 in the above-identified application. A Request for Oral Hearing is being filed concurrently.

I. STATUS OF CLAIMS

Claims 24-26, 28-32, 101, 105-108, 111-113, 115-121 and 124-160 are pending.

Claims 1-23, 27, 33-100, 102-104, 109, 110, 114, 122 and 123 were canceled. Claims 101, 117 and 151 are withdrawn from consideration as being drawn to non-elected species. Claims 24-26, 28-32, 105-108, 111-113, 115, 116, 118-121, 124-150, and 152-160 are rejected.

Claims 24-26, 28-32, 105-108, 111-113, 115, 116, 118-121, 124-150, and 152-160 are on appeal. A copy of the appealed claims appears in the Claims Appendix of the Amended Appeal Brief, filed on August 16, 2006.

II. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The rejection of claims 24-26, 28-32, 105-108, 111-113, 115, 116, 118-121, 124, 125, 136-150 and 152-160 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and use the invention has been withdrawn (Examiner's Answer at pages 2-3). This rejection was "Ground of Rejection B" in the Amended Appeal Brief. To comport with the Examiner's Answer, the Grounds of Rejection to be Reviewed on Appeal are labeled A, B and C in this Reply Brief.

A. Whether claims 24-26, 28-32, 105-108, 111-113, 115, 116, 118-121, 124, 125, 136-150 and 152-160 are properly rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that is not supported by adequate written description.

B. Whether claims 24-26, 28-31, 105-108, 111, 113, 115, 116, 118, 120, 121, 124, 126-142, 144-147, 149, 150, 152, 154, 155 and 157-160 are properly rejected under 35 U.S.C. § 103(a) as being obvious over Butcher *et al.* (WO 94/13312; Reference AD of record) in view of Vonderheide *et al.* (U.S. Patent No. 5,599,676; Reference AB of record) and Erle *et al.* (*J. Immunol.* 153:517-528 (1994); Reference AX3 of record). This ground of rejection was addressed as "Ground of Rejection C" in the Amended Appeal Brief.

C. Whether claims 32, 112, 119, 125, 143, 148, 153 and 156 are properly rejected under 35 U.S.C. § 103(a) as being obvious over Butcher *et al.* (WO 94/13312; Reference AD of record) in view of Vonderheide *et al.* (U.S. Patent No. 5,599,676, Reference AB of record) and Erle *et al.* (*J. Immunol.* 153:517-528 (1994); Reference AX3 of record), and further in view of Capon *et al.* (U.S. Patent No. 5,656,335; Reference AF of record). This ground of rejection was addressed as "Ground of Rejection D" in the Amended Appeal Brief.

III. ARGUMENT

Appellant maintains that the rejections should be reversed for the reasons stated in the Amended Appeal Brief. This Reply Brief addresses remarks and rationale in support of the rejections of record that were presented for the first time in the Examiner's Answer.

A. Response to Arguments Regarding Rejection of Claims 24-26, 28-32, 105-108, 111-113, 115, 116, 118-121, 124, 125, 136-150 and 152-160 under 35 U.S.C. 112, First Paragraph

Appellant thanks the Examiner for acknowledging that claim 103 was previously canceled.

The Examiner and conferees state that there is no disclosure in the specification as to which particular amino acid substitutions could be tolerated with the retention of the MAdCAM function, and that the Briskin declaration of November 19, 2001 demonstrates that it was unpredictable as to what residues could be substituted in MAdCAM without reducing or eliminating MAdCAM activity (Examiner's Answer, page 13).

Appellant maintains that the claims are supported by adequate written description for the reasons stated in the Amended Appeal Brief. The extensive exemplification and description of the invention in the specification, which sets forth the complete amino acid sequence of three species of naturally occurring primate MAdCAM, the conserved GLDTSL motif that is a common partial structure of naturally occurring primate MAdCAM and variant proteins that mediate $\alpha 4\beta 7$-dependent adhesion, a correlation between structure and $\alpha 4\beta 7$-dependent adhesion function, and exemplification of a fusion protein that comprises the extracellular domain of naturally occurring human MAdCAM, and a fusion protein that comprises the two N-terminal Ig domains of human MAdCAM, are adequate to convey to the person of skill in the art that Appellant was in possession of the claimed invention at the time the application was filed, even though particular amino acid substitutions are not provided (*See*, Amended Appeal Brief at VII.A., page 11 *et seq.*).

The Briskin declaration describes a study in which mutations were introduced into the CD and EF loops of domain 1 and into the CE and FG loops of domain 2 of human MAdCAM (Briskin Declaration, page 4 under "Mutagenesis of Individual Human MAdCAM-1 Residues"). The subject application teaches that domains 1 and 2 and the CD loop, are likely to be involved in $\alpha 4\beta 7$ binding (Specification at page 17, line 30 through page 22, line 24). Even though these areas are mutated, Dr. Briskin reports that about half of the 31 mutants assessed bound $\alpha 4\beta 7$ at levels between 80%-100% of control (Briskin Declaration at paragraph 5). Thus, the results described in the Briskin Declaration confirm the structure function relationship disclosed in the specification, by showing that domains 1 and 2 and the CD loop of primate MAdCAM are involved in $\alpha 4\beta 7$ binding.

B. Response to Arguments Regarding Rejection of Claims 24-26, 28-31, 105-108, 111, 113, 115, 116, 118, 120, 121, 124, 126-142, 144-147, 149, 150, 152, 154, 155 and 157-160 under 35 U.S.C. 103(a) over Butcher *et al.* in view of Vonderheide *et al.* and Erle *et al.*

The Examiner's Answer articulates the PTO's rationale for maintaining the rejection in view of Appellant's rebuttal argument for the first time, stating that the PTO does not read Bell and In re Deuel, 51 F.3d 1552, 34 USPQ2d 1210 (Fed. Cir. 1995) as setting forth a *per se* rule that so-called methodology cannot be taken into account in determining whether a given compound is obvious under 35 U.S.C. § 103(a) (Examiner's Answer, page 19). According to the Examiner's Answer the method described in Vonderheide *et al.* uses human cells expressing MAdCAM and $\alpha 4\beta 7$ to clone the desired nucleic acid and does not require any amino acid data from the protein of interest to be available (Examiner's Answer, page 21). In the Examiner and conferees' view, Vonderheide *et al.* provides evidence of the rapid advances in the art, and establishes that it would have been obvious to one of ordinary skill in the art to identify and isolate nucleic acids that encode adhesion molecules such as MAdCAM at the time of the present invention (Examiner's Answer, page 22).

Appellant's reliance on Deuel has been misconstrued. Appellant does not suggest that there is a *per se* rule prohibiting the consideration of technology that might be suitable for achieving a

result when determining whether the result is obvious. Rather, Deuel says that to make claimed fusion protein obvious, the art must suggest the claimed fusion protein itself to a person of ordinary skill in the art.

> Because Deuel claims new chemical entities in structural terms, a *prima facie* case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds* to a person of ordinary skill in the art.

Deuel, 51 F.3d at 1557, 34 USPQ2d at 1214.

Here, the art of record does not suggest the claimed fusion proteins because the cloning techniques disclosed in Vonderheide *et al.*, when combined with the teachings of Butcher *et al.* and Erle *et al.*, merely provide a general incentive and techniques that might have been used in a research program with the goal of arriving at the claimed invention. The combined teachings of the references do not suggest the particularly claimed fusion proteins themselves. It is well settled that the mere existence of a general incentive and techniques that are suitable to arrive at a claimed invention is not sufficient to establish a *prima facie* case of obviousness. In re Deuel, 51 F.3d at 1559, 34 USPQ2d at 1216. The Board has recognized and appropriately followed this mandatory authority in addressing the issue of obviousness.

> We are mindful of the holding in Bell, and the recently issued opinion In re Deuel, ...reaffirming the principle that a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question of whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs.

Ex parte Goldgaber, 41 USPQ2d 1172, 1176 (Bd. Pat. App. & Inter. 1995).

The Examiner and conferees appear to believe that this application can be distinguished from Deuel, because the method of Vonderheide *et al.* "does not require any amino acid data from the protein of interest to be available" (Examiner's Answer, page 21). However, this observation is further evidence that the references do not suggest the claimed fusion proteins to a person of

ordinary skill in the art. As described in the Amended Appeal Brief, the prior art in this application contains no amino acid sequence data, no nucleotide sequence data, and no other teachings that relate to the claimed fusion proteins (*See*, Amended Appeal Brief at VII.C.2.a. pages 38-39). Accordingly, the prior art in this application places the person of ordinary skill in the art further away from the claimed invention than he was in Deuel, with nothing to point him toward the claimed fusion proteins.

Perhaps the Examiner and conferees think that it would have been obvious to use Vonderheide's method in an attempt to make the claimed invention. However, even though the method of Vonderheide *et al.* is presumed to be enabled, the combined teachings of Butcher *et al.*, Erle *et al.*, and Vonderheide *et al.* merely create a research plan with uncertainty as to whether a nucleic acid encoding a naturally occurring primate MAdCAM, or fragment thereof, as claimed would be identified. An obvious approach to try rationale is not sufficient to create a *prima facie* case against the claimed fusion proteins. (MPEP § 2145 (X(B)) 8th ed., Rev. Aug. 2006.)

The prior art only teaches murine MAdCAM, which has limited sequence similarity to primate MAdCAM (Butcher *et al.*), a belief that human or primate MAdCAM is likely to exist and bind α4β7 integrin (Erle *et al.*), and the existence of a possible method for cloning receptors for α4 integrins (Vonderheide *et al.*). Therefore, the rejection should be reversed because the combined teachings of Butcher *et al.*, Erle *et al.*, and Vonderheide *et al.* merely amount to a research plan that one of skill in the art might have utilized in an attempt to discover a receptor for an α4 integrin, and do not suggest or provide a reasonable expectation of success in producing the particular claimed fusion proteins.

C. Response to Arguments Regarding Rejection of Claims 32, 112, 119, 125, 143, 148, 153 and 156 under 35 U.S.C. § 103(a) over Butcher *et al.*, in view of Vonderheide *et al.*, Erle *et al.* and further in view of Capon *et al.*

The Examiner's Answer did not present any new remarks in support of the rejections of record. Appellant maintains that the rejection should be reversed for the reasons stated in the Amended Appeal Brief, and the reasons stated above with respect to "Ground of Rejection B."

CONCLUSION

In view of the foregoing and the arguments presented in the Amended Appeal Brief filed on August 16, 2006 reversal of the rejections is requested.

Respectfully submitted,

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